

BATCH **COMPLETE**
PROJECTED ITERATIONS: 561 TO 1399
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 17:00:06 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1061 TO ITERATE

100.0% PROCESSED 1061 ITERATIONS
SEARCH TIME: 00.00.01

27 ANSWERS

L3 27 SEA SSS FUL L1

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COST IN U.S. DOLLARS

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TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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140.49

FILE 'CAPLUS' ENTERED AT 17:00:14 ON 16 JUL 2002

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FILE COVERS 1907 - 16 Jul 2002 VOL 137 ISS 3

FILE LAST UPDATED: 15 Jul 2002 (20020715/ED)

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L4 12 L3

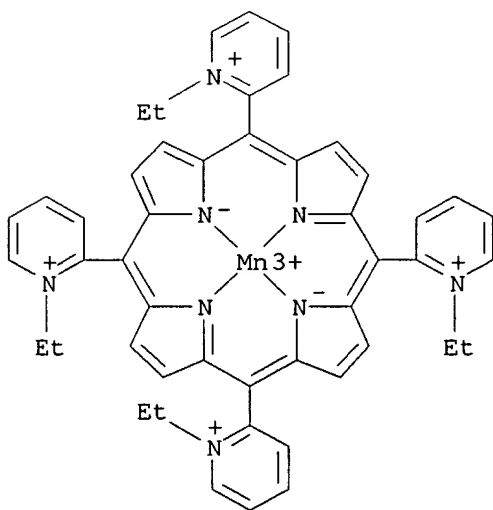
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L4 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2002 ACS

Habte

~~06/27/2002~~
7/16/02

ACCESSION NUMBER: 2002:102984 CAPLUS
 DOCUMENT NUMBER: 136:278003
 TITLE: A metalloporphyrin-based superoxide dismutase mimic
 inhibits adoptive transfer of autoimmune diabetes by
 a
 diabetogenic T-cell clone
 AUTHOR(S): Piganelli, Jon D.; Flores, Sonia C.; Cruz, Coral;
 Koepp, Jeffrey; Batinic-Haberle, Ines; Crapo, James;
 Day, Brian; Kachadourian, Remy; Young, Rebekah;
 Bradley, Brenda; Haskins, Kathryn
 CORPORATE SOURCE: Department of Immunology, University of Colorado
 Health Sciences Center and Barbara Davis Center for
 Childhood Diabetes, Denver, CO, USA
 SOURCE: Diabetes (2002), 51(2), 347-355
 CODEN: DIAEAZ; ISSN: 0012-1797
 PUBLISHER: American Diabetes Association
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 223723-79-3, AEOL 10113
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (AEOL 10113; metalloporphyrin-based superoxide dismutase mimic
 inhibits
 adoptive transfer of autoimmune diabetes by a diabetogenic T-cell
 clone)
 RN 223723-79-3 CAPLUS
 CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
 .kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
 ethylpyridiniumato]](2-)]-, (SP-4-1)-(9CI) (CA INDEX NAME)



AB We present here the first report of a metalloporphyrin-based antioxidant
 that can prevent or delay the onset of autoimmune diabetes. Type 1
 diabetes is an autoimmune process whereby T-cells recognize pancreatic

.beta.-cell antigens and initiate a leukocyte infiltrate that produces proinflammatory cytokines and reactive oxygen species (ROS), ultimately leading to .beta.-cell destruction. Because islet .beta.-cells have a reduced capacity to scavenge free radicals, they are very sensitive to ROS action. Metalloporphyrin-based superoxide dismutase (SOD) mimics scavenge ROS and protect cells from oxidative stress and apoptosis. To investigate the effect of SOD mimics and the role of oxidative stress in the development of autoimmune diabetes in vivo, we used a diabetogenic T-cell clone, BDC-2.5, to induce rapid onset of diabetes in young nonobese diabetic-severe combined immunodeficient mice (NOD.scid). Disease was significantly delayed or prevented altogether by treatment of recipient mice with an SOD mimic, AEOL-10113, before transfer of the BDC-2.5 clone. To investigate the mechanisms of protection, in vitro assays for T-cell proliferation and .gamma.-interferon (IFN-.gamma.) prodn. were carried out using the T-cell clone BDC-2.5. We found that the SOD mimic significantly inhibited antigen-presenting cell-dependent T-cell proliferation and IFN-.gamma. prodn. in vitro. In addn., pretreatment of lipopolysaccharide (LPS)-stimulated peritoneal macrophages with SOD mimic inhibited the LPS-dependent increase in TNF-.alpha. as well as the NADPH oxidase-dependent release of superoxide. Finally, this compd. protected NIT-1 insulinoma cells from interleukin-1.beta. and alloxan cytotoxicity in vitro.

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

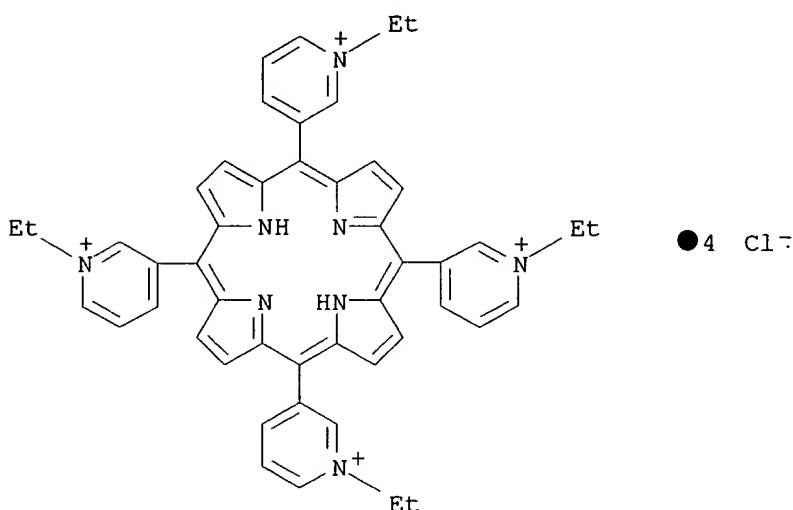
L4 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:861184 CAPLUS
DOCUMENT NUMBER: 136:151025
TITLE: Quadraplex-Interactive Agents as Telomerase Inhibitors: Synthesis of Porphyrins and Structure-Activity Relationship for the Inhibition of Telomerase
AUTHOR(S): Shi, Dong-Fang; Wheelhouse, Richard T.; Sun, Daekyu; Hurley, Laurence H.
CORPORATE SOURCE: College of Pharmacy, University of Texas at Austin, Austin, TX, 78712, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(26), 4509-4523
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 211360-11-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis of porphyrins and their structure-activity relationship for the inhibition of telomerase)

RN 211360-11-1 CAPLUS

CN Pyridinium,

3,3',3'',3'''-(21H,23H-porphine-5,10,15,20-tetrayl)tetrakis[1-ethyl-, tetrachloride (9CI) (CA INDEX NAME)



AB The cationic 5,10,15,20-tetrakis(1-methylpyridinium-4-yl)porphyrin (TMPyP4) binds to quadruplex DNA and is thereby an inhibitor of human telomerase (Wheelhouse et al. J. Am. Chem. Soc. 1998, 120, 3261-3262). The synthesis and telomerase-inhibiting activity of a wide range of analogs of TMPyP4 were reported, from which rules for a structure-activity relationship (SAR) have been discerned: (1) stacking interactions are crit. for telomerase inhibition, (2) pos. charged substituents are important but may be interchanged and combined with hydrogen-bonding groups, and (3) substitution is tolerated only on the meso positions of the porphyrin ring, and the bulk of the substituents should be matched to the width of the grooves in which they putatively lie. This SAR is consistent with a model presented for the complexation of TMPyP4 with human telomeric quadruplex DNA.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

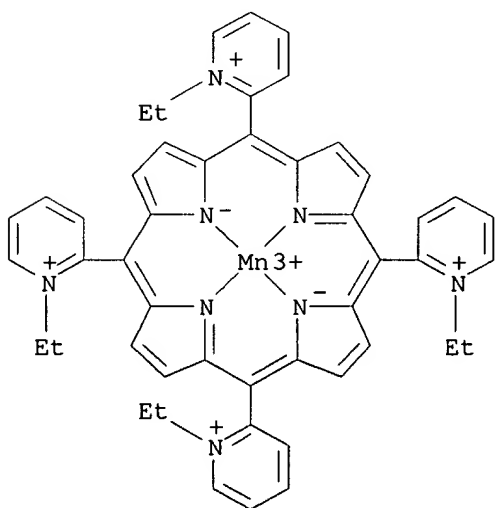
L4 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:462721 CAPLUS

DOCUMENT NUMBER: 135:283070

TITLE: Neuroprotection from delayed postischemic administration of a metalloporphyrin catalytic antioxidant

AUTHOR(S): Mackensen, G. Burkhard; Patel, Manisha; Sheng, Huaxin;
Calvi, Carla L.; Batinic-Haberle, Ines; Day, Brian J.;
Liang, Li Ping; Fridovich, Irwin; Crapo, James D.; Pearlstein, Robert D.; Warner, David S.
CORPORATE SOURCE: Department of Anesthesiology, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Journal of Neuroscience (2001), 21(13), 4582-4592
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 223723-79-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(neuroprotection from delayed postischemic administration of a metalloporphyrin catalytic antioxidant)
RN 223723-79-3 CAPLUS
CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



AB Reactive oxygen species contribute to ischemic brain injury. This study examd. whether the porphyrin catalytic antioxidant manganese (III) meso-tetrakis (N-ethylpyridinium-2-yl)porphyrin (MnTE-2-PyP5+) reduces oxidative stress and improves outcome from exptl. cerebral ischemia.
Rats that were subjected to 90 min focal ischemia and 7 d recovery were given

MnTE-2-PyP5+ (or vehicle) intracerebroventricularly 60 min before ischemia, or 5 or 90 min or 6 or 12 h after reperfusion. Biomarkers of brain oxidative stress were measured at 4 h after postischemic treatment (5 min or 6 h). MnTE-2-PyP5+, given 60 min before ischemia, improved neurol. scores and reduced total infarct size by 70%. MnTE-2-PyP5+, given 5 or 90 min after reperfusion, reduced infarct size by 70-77% and had no effect on temp. MnTE-2-PyP5+ treatment 6 h after ischemia reduced total infarct vol. by 54% (vehicle, 131 +/- 60 mm3; MnTE-2-PyP5+, 300 ng, 60 +/- 68 mm3). Protection was obsd. in both cortex and caudoputamen, and neurol. scores were improved. No MnTE-2-PyP5+ effect was obsd. if it was given 12 h after ischemia. MnTE-2-PyP5+ prevented mitochondrial aconitase inactivation and reduced 8-hydroxy-2'-deoxyguanosine formation when it was given 5 min or 6 h after ischemia. In mice, MnTE-2-PyP5+ reduced infarct size and improved neurol. scores when it was given i.v. 5 min after ischemia. There was no effect of 150 or 300 ng of MnTE-2-PyP5+ pretreatment on selective neuronal necrosis resulting from 10 min forebrain ischemia and 5 d recovery in rats. Administration of a metalloporphyrin catalytic antioxidant had marked neuroprotective effects against focal ischemic insults when it was given up to 6 h after ischemia. This was assocd. with decreased postischemic superoxide-mediated oxidative stress.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:395533 CAPLUS

DOCUMENT NUMBER: 135:187164

TITLE: An LDI-TOF and ESI mass spectrometry study of a series

AUTHOR(S): of .beta.-substituted cationic metalloporphyrins
Kachadourian, R.; Srinivasan, N.; Haney, C. A.;
Stevens, R. D.

CORPORATE SOURCE: Department of Medicine, National Jewish Medical and
Research Center, Denver, CO, 80206, USA

SOURCE: Journal of Porphyrins and Phthalocyanines (2001),
5(6), 507-511
CODEN: JPPHFZ; ISSN: 1088-4246

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 219818-60-7 219818-61-8 219818-62-9

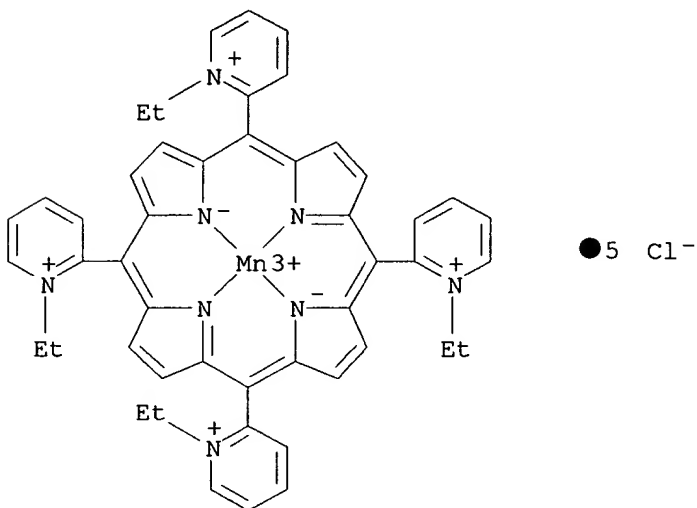
219818-63-0 219818-64-1 355117-69-0

RL: PRP (Properties)

(LDI-TOF and ESI mass spectrometry study of series of
.beta.-halogenated cationic metalloporphyrins)

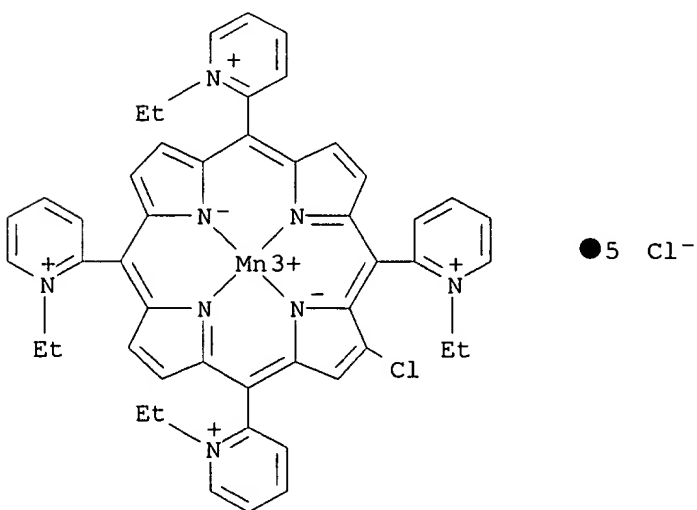
RN 219818-60-7 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



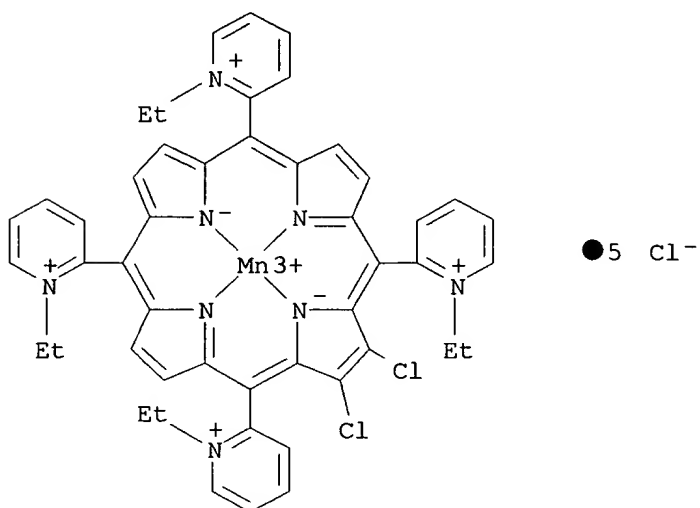
RN 219818-61-8 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2-chloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 219818-62-9 CAPLUS

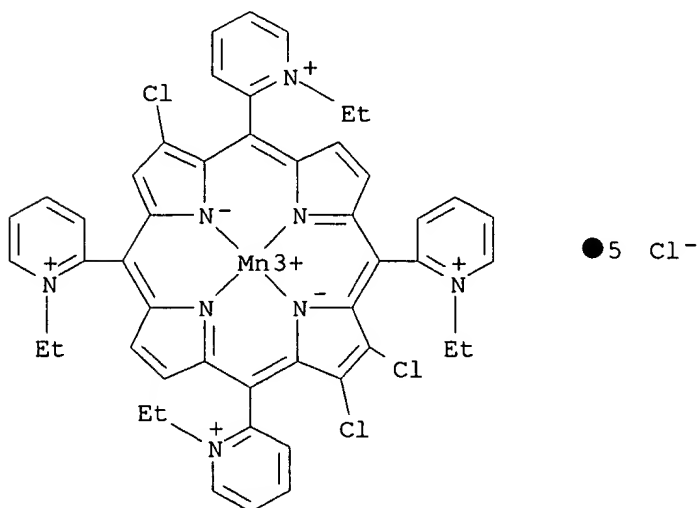
CN Manganese(5+), [[2,2',2'',2'''-(2,3-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)

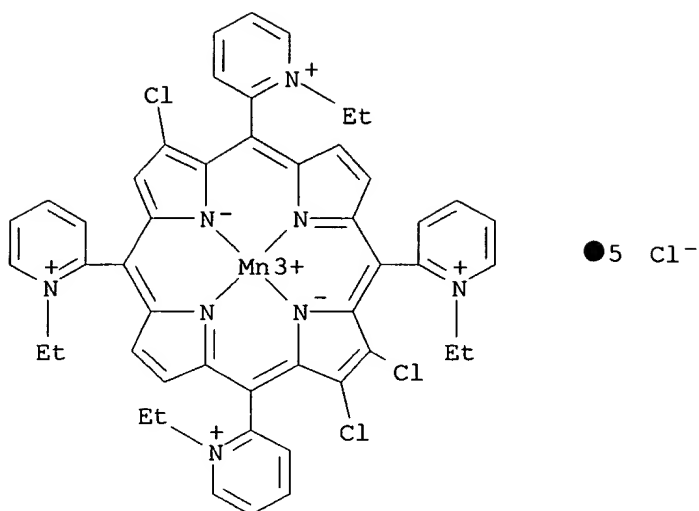


RN 219818-63-0 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2,3,12-trichloro-21H,23H-porphine-

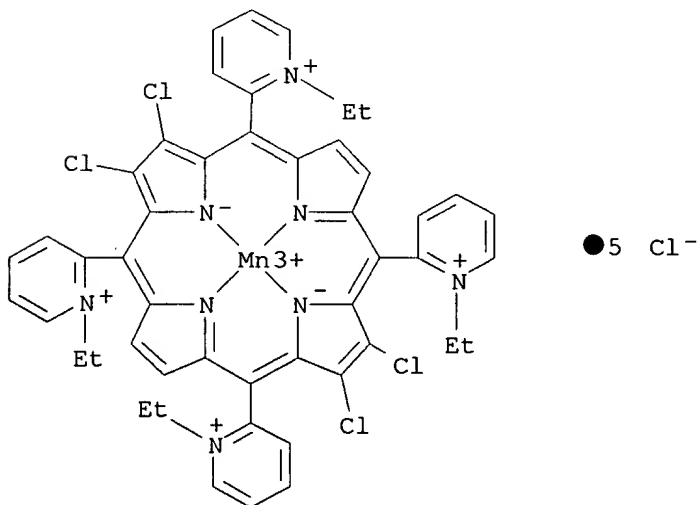
5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)





RN 219818-64-1 CAPLUS

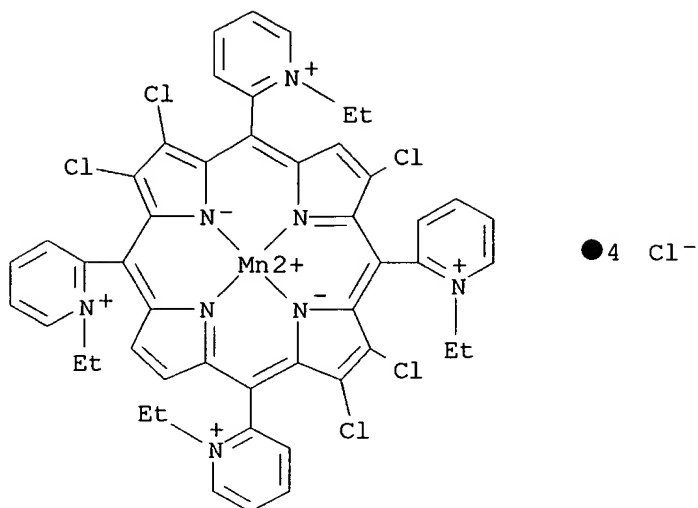
CN Manganese(5+), [[2,2',2'',2'''-(2,3,12,13-tetrachloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 355117-69-0 CAPLUS

CN Manganese(4+), [[2,2',2'',2'''-(2,3,7,12,13-pentachloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, tetrachloride, (SP-4-2)- (9CI) (CA INDEX NAME)

NAME)



AB A series of .beta.-halogenated cationic metalloporphyrins were analyzed by LDI-TOF and ESI-MS. Although LDI-TOFMS proves to be a good tool for the characterization of this family of metal complexes, including the redox state of the metal, ESI-MS indicates in addn. the relative tendency of such metal complexes to be reduced.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:372677 CAPLUS
 DOCUMENT NUMBER: 135:253633
 TITLE: Manganese(III) complexes with porphyrins and related compounds as catalytic scavengers of superoxide
 AUTHOR(S): Spasojevic, I.; Batinic-Haberle, I.
 CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, NC, 27710, USA
 SOURCE: Inorganica Chimica Acta (2001), 317(1,2), 230-242
 CODEN: ICHAA3; ISSN: 0020-1693
 PUBLISHER: Elsevier Science S.A.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 223723-79-3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); PRP (Properties); BIOL (Biological study); USES (Uses) (superoxide dismutase mimic; manganese(III) complexes with porphyrins)

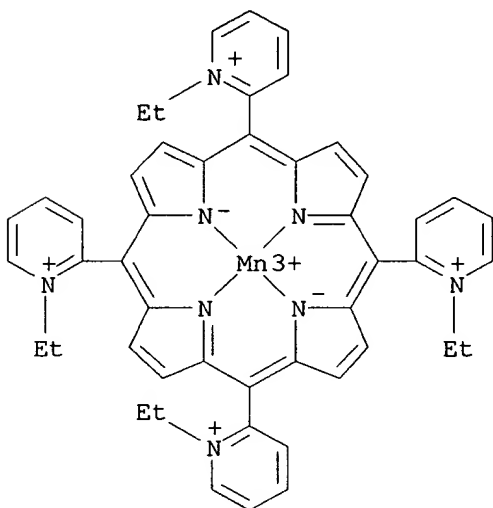
Habte

<06/27/2002

and related compds. as catalytic scavengers of superoxide)

RN 223723-79-3 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



AB Two groups of Mn-based catalytic antioxidants are described in terms of their catalytic activities and electrochem. properties. In the first group, manganese porphyrins, phthalocyanine, and porphyrazine employ the Mn(III)/Mn(II) couple in the catalysis of O₂.bul.- dismutation (disproportionation). The catalytic rate const. is dependent upon the metal-centered redox potential, as shown previously for water-sol. Mn porphyrins. The limitation of this simple relation becomes obvious with compds. of high redox potential (+2 metal oxidn. state is stabilized) which exhibit a weak metal/ligand binding; although of high superoxide dismutase (SOD)-like activity, the compds. are not stable under physiol. conditions. The second generation of the potent O₂.bul.- scavengers are manganese complexes with biliverdin IX and its derivs. which have an RO-functionality as a fifth coordination to the metal center in a dimeric structure. Such a coordination pattern stabilizes the +4 oxidn. state of the manganese so that the Mn(III)/Mn(IV) redox (E_{1/2}=apprx.+0.46 V vs. NHE) becomes coupled to the O₂.bul.- dismutation. More importantly, despite operating at a high pos. metal-centered redox potential and having the +3 oxidn. state as the resting state of the metal center, metallobiliverdins still retain a high ligand affinity in soln. Independently of their charge (two neutral and the other two neg. charged) metallobiliverdins studied are of similar SOD-like activity comparable to the efficacy of highly charged manganese(III) ortho N-alkylpyridylporphyrins. These most potent in vitro SOD-like Mn porphyrins

are also reactive toward peroxyxynitrite, nitric oxide, hydrogen peroxide and oxygen. Since the fifth coordination site of the metal center is occupied no reactivity of the manganese(III) biliverdin IX di-Me ester toward NO.bul. and H2O2 is obsd. Thus, manganese(III) porphyrins and manganese(III) biliverdins are expected to differ with regard to their tissue localization and to the type and the concn. of reactive oxygen species they would encounter in biol. systems. Comparative kinetic and thermodyn. studies of these catalytic antioxidants would help us understand

not only the prevalent mode of their in vivo biol. action but the mechanism of oxidative stress injuries as well.

REFERENCE COUNT: 115 THERE ARE 115 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:701449 CAPLUS

DOCUMENT NUMBER: 134:128032

TITLE: Nitrosylation of Manganese(II) Tetrakis(N-ethylpyridinium-2-yl)porphyrin: A Simple and

Sensitive

AUTHOR(S): Spectrophotometric Assay for Nitric Oxide
Spasojevic, Ivan; Batinic-Haberle, Ines; Fridovich, Irwin

CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, NC, 27710, USA

SOURCE: Nitric Oxide (2000), 4(5), 526-533

CODEN: NIOXF5; ISSN: 1089-8603

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

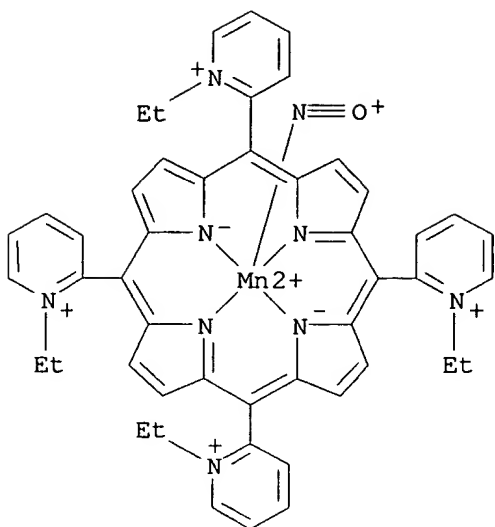
LANGUAGE: English

IT 321839-25-2

RL: ANT (Analyte); FMU (Formation, unclassified); PRP (Properties); ANST (Analytical study); FORM (Formation, nonpreparative)
(nitrosylation of manganese(II) tetrakis(N-ethylpyridinium-2-yl)porphyrin as a simple and sensitive spectrophotometric assay for nitric oxide)

RN 321839-25-2 CAPLUS

CN Manganese(5+), nitrosyl[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)- (9CI) (CA INDEX NAME)

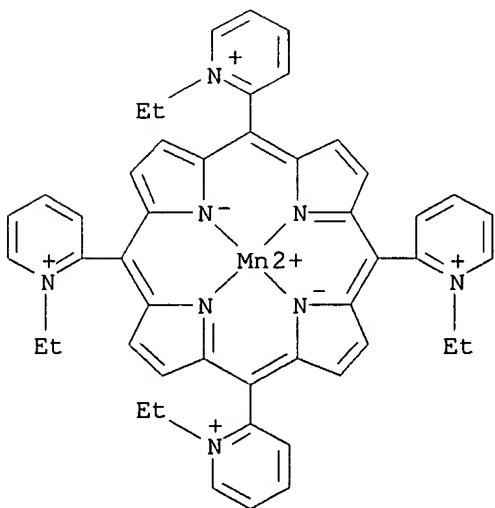


IT 223723-81-7

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (nitrosylation of manganese(II) tetrakis(N-ethylpyridinium-2-yl)porphyrin as a simple and sensitive spectrophotometric assay for nitric oxide)

RN 223723-81-7 CAPLUS

CN Manganese(4+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



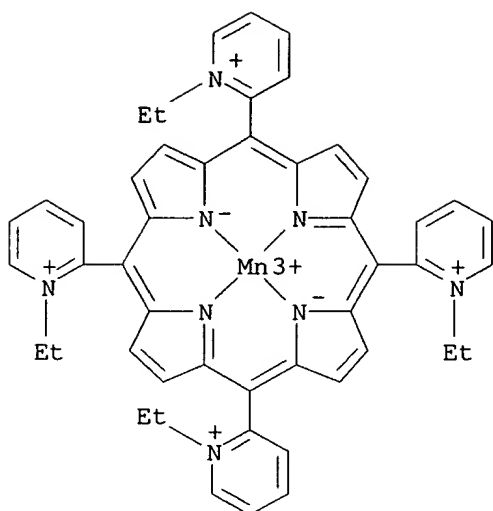
AB Reaction between NO.bul. and manganese tetrakis(N-ethylpyridinium-2-yl)porphyrin (MnIIITE-2-PyP5+) was investigated at 25.degree.. At high

excess of NO.bul. (1.5 mM) the reaction with the oxidized, air-stable form MnIIITE-2-PyP5+ (5 .mu.M), proceeds very slowly (t1/2 .simeq. 60 min). The presence of excess ascorbate (1 mM) produces the reduced form, MnIITE-2-PyP4+, which reacts with NO.bul. stoichiometrically and in the time of mixing (k .simeq. 1.times.106 M-1 s-1). The high rate of formation and the stability of the product, MnIITE-2-PyP(NO)4+ ({Mn(NO)}6), make the reaction out compete the reaction of NO.bul. with O2. Our in vitro measurements show a linear absorbance response upon addn. of NO to a PBS, pH 7.4, soln. contg. an excess of ascorbate over MnIIITE-2-PyP5+. Thus, the obsd. interactions can be the basis of a convenient and sensitive spectrophotometric assay for NO.bul.. Also, it may have important implications for the in vivo behavior of MnIIITE-2-PyP5+ which is currently exploited as a possible therapeutic agent for various oxygen-radical related disorders. (c) 2000 Academic Press.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS

FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:364350 CAPLUS
 DOCUMENT NUMBER: 133:248491
 TITLE: Manganese-porphyrin reactions with lipids and lipoproteins
 AUTHOR(S): Bloodsworth, A.; O'Donnell, V. B.; Batinic-Haberle, I.; Chumley, P. H.; Hurt, J. B.; Day, B. J.; Crow, J. P.; Freeman, B. A.
 CORPORATE SOURCE: Center for Free Radical Biology, Departments of Anesthesiology, Biochemistry and Molecular Genetics, Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, AL, USA
 SOURCE: Free Radical Biology & Medicine (2000), 28(7), 1017-1029
 CODEN: FRBMEH; ISSN: 0891-5849
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 223723-79-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (manganese-porphyrin reactions with linoleic acid emulsions, human plasma low-d. lipoproteins and brain tissue homogenates)
 RN 223723-79-3 CAPLUS
 CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



AB Manganese porphyrin complexes serve to catalytically scavenge superoxide, hydrogen peroxide, and peroxynitrite. Herein, reactions of manganese 5,10,15,20-tetrakis(N-ethylpyridinium-2-yl)porphyrin (MnTE-2-PyP5+) with lipids and lipid hydroperoxides (LOOH) are examd. In linoleic acid and human low-d. lipoprotein (LDL), MnTE-2-PyP5+ promotes oxidative reactions when biol. reductants are not present. By redox cycling between Mn+3 and Mn+4 forms, MnTE-2-PyP5+ initiates lipid peroxidn. via decompn. of 13(S)hydroperoxyoctadecadienoic acid [13(S)HPODE], with a second-order rate const. of 8.9 .times. 10³ M⁻¹s⁻¹ and kcat = 0.32 s⁻¹. Studies of LDL oxidn. demonstrate that: (i) MnTE-2-PyP5+ can directly oxidize LDL, (ii) MnTE-2-PyP5+ does not inhibit Cu-induced LDL oxidn., and (iii) MnTE-2-PyP5+ plus a reductant partially inhibit lipid peroxidn. MnTE-2-PyP5+ (1-5 .mu.M) also significantly inhibits FeCl₃ plus ascorbate-induced lipid peroxidn. of rat brain homogenate. In summary, MnTE-2-PyP5+ initiates membrane lipid and lipoprotein oxidn. in the absence of biol. reductants, while MnTE-2-PyP5+ inhibits lipid oxidn. reactions initiated by other oxidants when reductants are present. It is proposed that, as the Mn+3 resting redox state of MnTE-2-PyP5+ becomes oxidized to the Mn+4 redox state, LOOH is decompd. to byproducts that propagate lipid oxidn. reactions. When the manganese of MnTE-2-PyP5+ is reduced to the +2 state by biol. reductants, antioxidant reactions of the metalloporphyrin are favored.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

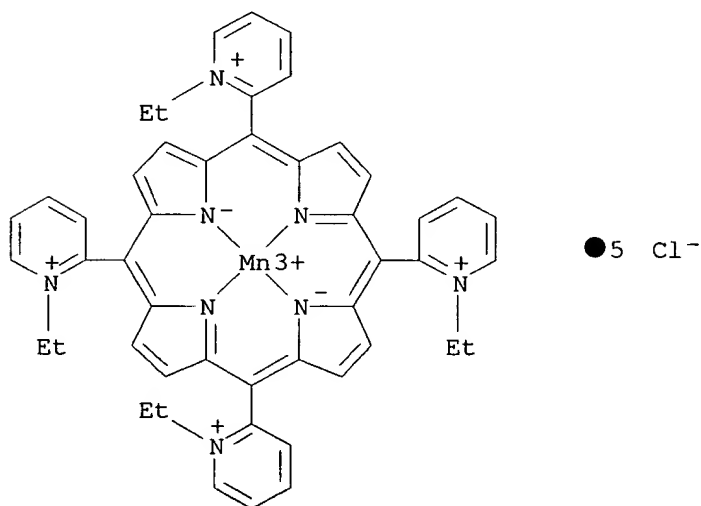
L4 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:251138 CAPLUS

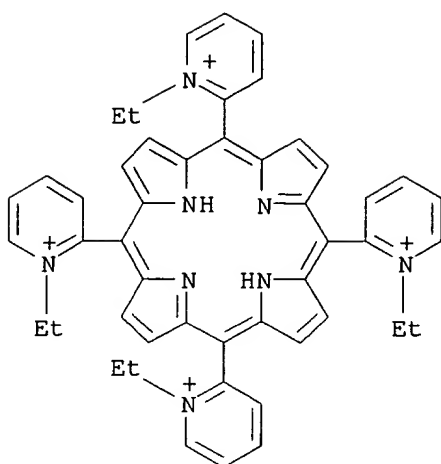
DOCUMENT NUMBER: 132:340751

TITLE: Electrospray mass spectrometry of isomeric tetrakis(N-alkylpyridyl)porphyrins and their manganese(III) and iron(III) complexes

AUTHOR(S): Batinic-Haberle, Ines; Stevens, Robert D.; Fridovich, Irwin
 CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, NC, 27710, USA
 SOURCE: Journal of Porphyrins and Phthalocyanines (2000), 4(3), 217-227
 CODEN: JPPHFZ; ISSN: 1088-4246
 PUBLISHER: John Wiley & Sons Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 219818-60-7 223723-78-2
 RL: PRP (Properties)
 (electrospray mass spectrometry of isomeric tetrakis(N-alkylpyridyl)porphyrins and manganese(III) and iron(III) complexes)
 RN 219818-60-7 CAPLUS
 CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)-(9CI) (CA INDEX NAME)



RN 223723-78-2 CAPLUS
 CN Pyridinium,
 2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl)tetrakis[1-ethyl-, tetrachloride (9CI) (CA INDEX NAME)



● 4 Cl⁻

AB Mn(III) complexes of isomeric tetrakis(N-alkylpyridyl)porphyrins (N-alkyl = N-Me, M or N-Et, E), MnTM(E)-2(3,4)-PyP5⁺, are being developed as superoxide dismutase (SOD) mimics. Simultaneously, techniques for their purifn., identification and characterization are being pursued. Electrospray mass spectrometry (ESMS) proved to be an excellent method for identification and characterization of this group of H₂O-sol. cationic porphyrins. The multiply charged parent ion is obsd. for both the metal-free ligands and their corresponding Mn complexes. The other major peaks in the mass spectra result from loss of N-alkyl groups, redn. of the metal center, axial coordination of chloride or hydroxo ion in the case of the Fe porphyrin, loss of metal and deprotonation of pyrrolic nitrogens. As a result of inductive and resonance effects, which stabilize the ortho isomer, almost no loss of N-alkyl groups from the Mn complex or from its parent ligand was obsd. The relative intensity of the multiply charged mol. ion MnIIITM-3(4)-PyP5⁺/5 was 100% in the case of the meta and para isomers. Although Mn porphyrins display a low preference toward axial ligation, favorable electrostatics at the metal center of the ortho isomer gives rise to 100% relative intensity of the species that has chloride axially ligated at the Mn site, MnIIITM(E)-2-PyPCl4⁺/4. When the stronger preference of Fe porphyrins toward axial ligation combines with the ortho effect, the monohydroxo Fe porphyrin FeIIITM-2-PyP(OH)4⁺/4 dominates the ESMS of an aq. MeCN soln. at pH 7.8.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:510816 CAPLUS

DOCUMENT NUMBER: 131:251645

TITLE: Relationship among Redox Potentials, Proton
Dissociation Constants of Pyrrolic Nitrogens, and in
Vivo and in Vitro Superoxide Dismutating Activities

of

AUTHOR(S): Manganese(III) and Iron(III) Water-Soluble Porphyrins
Batinic-Haberle, Ines; Spasojevic, Ivan; Hambright,
Peter; Benov, Ludmil; Crumbliss, Alvin L.; Fridovich,
IrwinCORPORATE SOURCE: Department of Biochemistry, Duke University Medical
Center, Durham, NC, 27710, USA

SOURCE: Inorganic Chemistry (1999), 38(18), 4011-4022

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

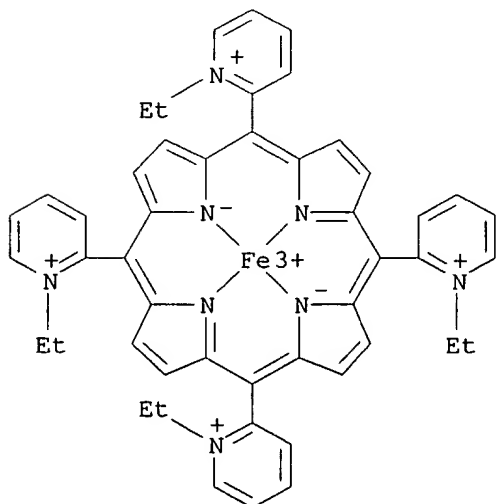
DOCUMENT TYPE: Journal

LANGUAGE: English

IT 244181-39-3

RL: RCT (Reactant); RACT (Reactant or reagent)
(addn. of water and hydroxide and methylimidazole)

RN 244181-39-3 CAPLUS

CN Iron(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)

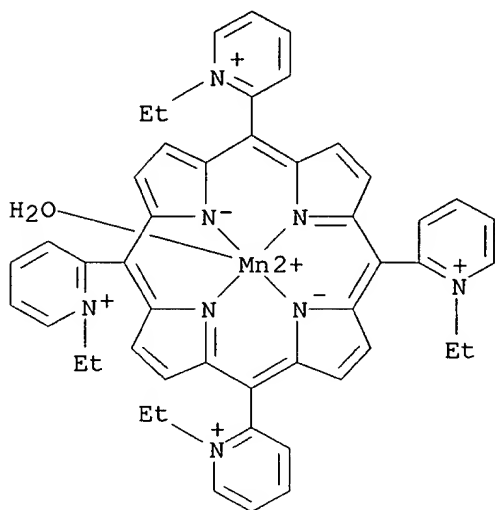
IT 244181-02-0 244181-17-7 244181-24-6

RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation,
nonpreparative)

(elec. potential of couple contg.)

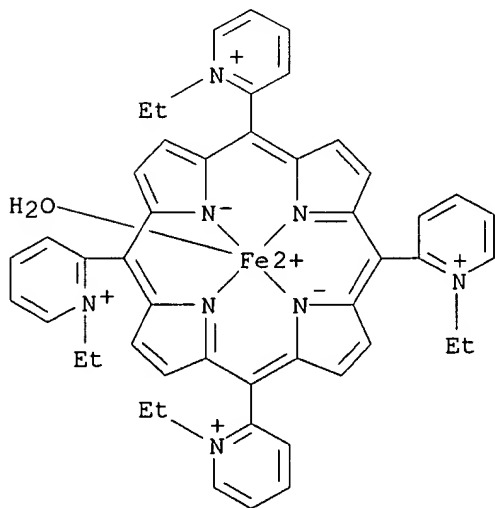
RN 244181-02-0 CAPLUS

CN Manganese(4+), aqua[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)-(9CI) (CA INDEX NAME)



RN 244181-17-7 CAPLUS

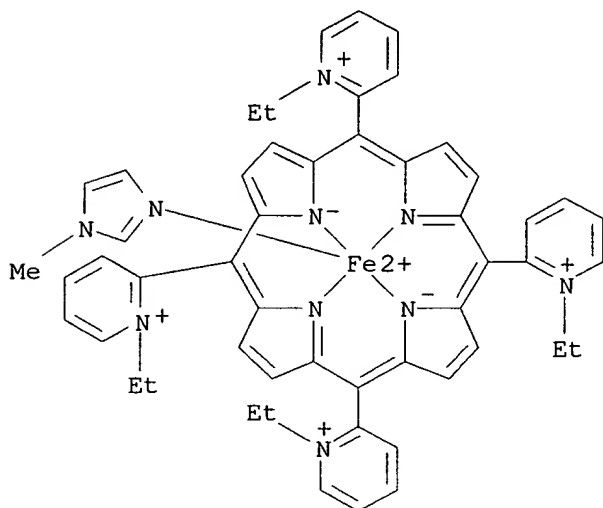
CN Iron(4+), aqua[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)-(9CI) (CA INDEX NAME)



RN 244181-24-6 CAPLUS

CN Iron(4+), (1-methyl-1H-imidazole-.kappa.N3)[[2,2',2'',2'''-(21H,23H-

porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetra-
kakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)- (9CI) (CA INDEX NAME)

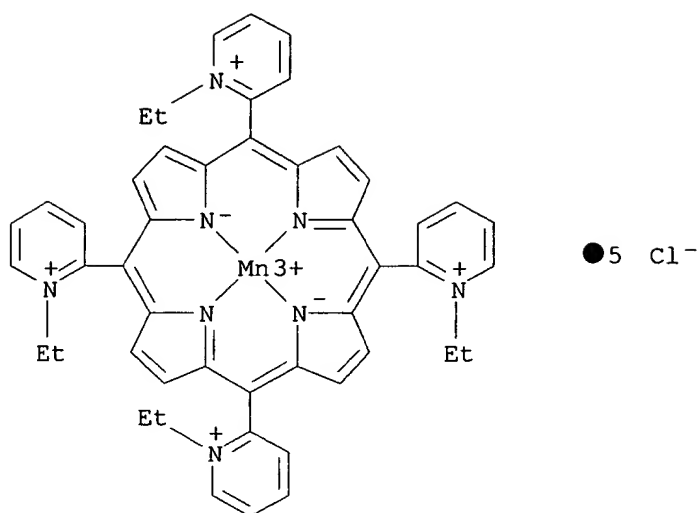


IT **219818-60-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and addn. of water and hydroxide)

RN 219818-60-7 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX
NAME)

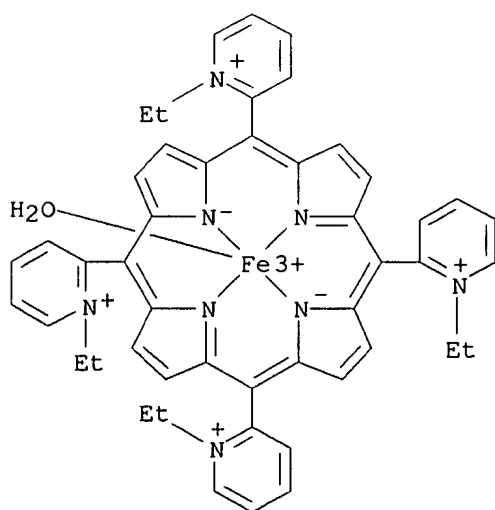


IT **244180-85-6P**

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and cyclic voltammetry)

RN 244180-85-6 CAPLUS

CN Iron(5+), aqua[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)- (9CI) (CA INDEX NAME)



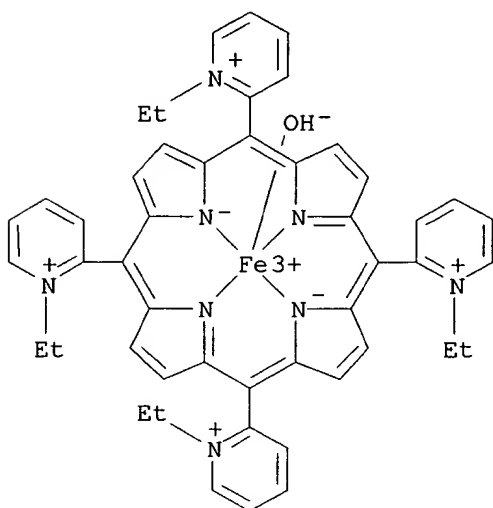
IT **244180-89-0P 244180-94-7P**

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and cyclic voltammetry and inhibition of cytochrome c redn. by superoxide)

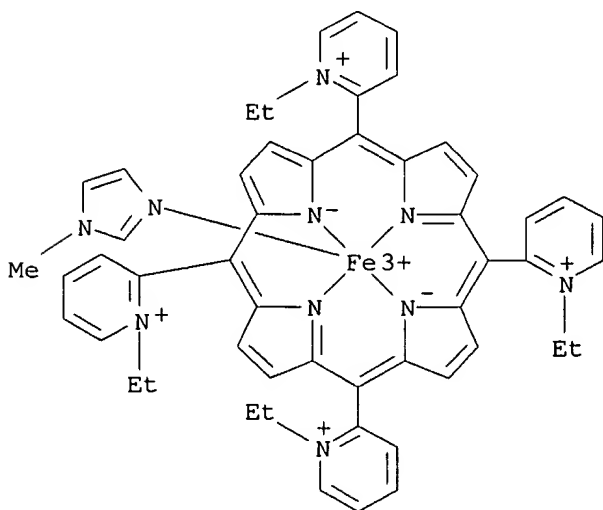
RN 244180-89-0 CAPLUS

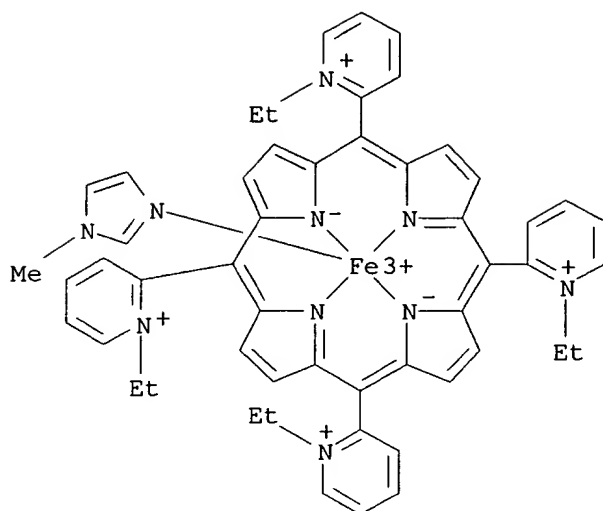
CN Iron(4+), hydroxy[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)- (9CI) (CA INDEX NAME)



RN 244180-94-7 CAPLUS

CN Iron(5+), (1-methyl-1H-imidazole-.kappa.N3)[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-5-12)- (9CI) (CA INDEX NAME)



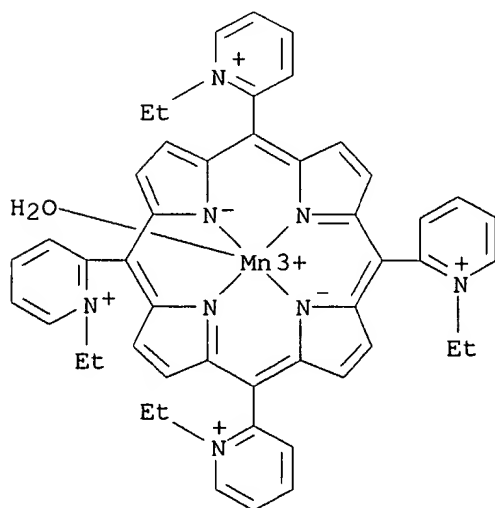


IT **244180-70-9P**

RL: CAT (Catalyst use); PEP (Physical, engineering or chemical process);
 PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
 (Preparation); PROC (Process); RACT (Reactant or reagent); USES (Uses)
 (prepn. and cyclic voltammetry and oxidative degrdn. by hydrogen
 peroxide and inhibition of cytochrome c redn. by superoxide)

RN 244180-70-9 CAPLUS

CN Manganese(5+), aqua[[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
 .kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
 ethylpyridiniumato]](2-)]-, (SP-5-12)-(9CI) (CA INDEX NAME)



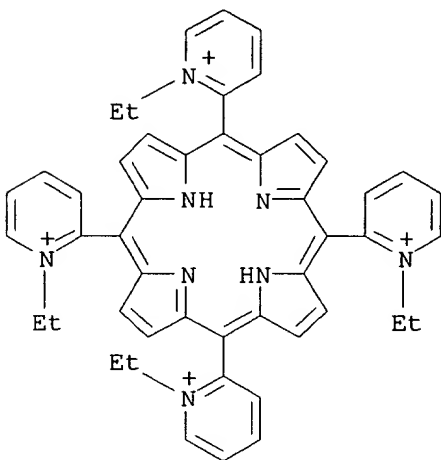
IT **223723-78-2P**

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and dissocn. consts. and complexation with iron and manganese)

RN 223723-78-2 CAPLUS

CN Pyridinium,

2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl)tetrakis[1-ethyl-, tetrachloride (9CI) (CA INDEX NAME)



●4 Cl⁻

AB Several Fe(III) and Mn(III) porphyrin complexes were prepd. The log kcat values for the dismutation of O₂.bul.- by monohydroxoiron(III) and aquamanganese(III) porphyrins, including ortho, meta, and para isomers of 5,10,15,20-tetrakis(N-alkylpyridiniumyl)porphyrins, vary linearly with the

metal-centered redox potentials (E_{1/2}) for the M(III)/M(II) couple. Each 120 mV increase in E_{1/2} imparted a 10-fold increase in kcat. The obsd. behavior is in accord with the Marcus equation for outer-sphere electron-transfer reactions, suggesting that the same mechanism is operative for Fe and Mn porphyrins. The Marcus plot enabled the authors to est. the self-exchange rate consts. of monohydroxoiron porphyrins to be

.apprx.1 order of magnitude higher than those of aquamanganese porphyrins.

also, E_{1/2} values for all of the metalloporphyrins studied were linearly related to the acid dissocn. consts. (pK_{a3}) of the pyrrolic N of the metal-free porphyrins, indicating that either E_{1/2}, or the more readily measured pK_{a3}, may be useful in predicting SOD activity in vitro. The most potent compds. studied, with respect to SOD activity, are those of the ortho N-alkylpyridiniumyl series. Ortho N-alkylpyridiniumyl groups are more electron withdrawing than are the meta or para groups, thus

imparting a more pos. redox potential and a correspondingly higher SOD activity. Sufficiently pos. potentials, or sufficiently low pKa3 values, are necessary for useful SOD activity, but so is the absence of toxicity. Despite their favorable redox potentials and SOD activities, all Fe(III) porphyrins studied were toxic to E. coli under both aerobic and anaerobic conditions and to both SOD-deficient and SOD-proficient strains. Only

the

ortho and meta Mn isomers of the N-alkylpyridiniumyl series (MnIIITE-2-PyP5+, MnIIITM-2-PyP5+ and MnIIITM-3-PyP5+) significantly protected SOD-deficient E. coli and allowed growth in an aerobic minimal medium. In previous work, the lower toxicity of these compds. is due to diminished ability to bind to nucleic acids. The Mn(III) complexes are preferable to the Fe(III) complexes for SOD mimics possibly due to a

lower

tendency for axial ligation. The authors propose E1/2 .gtoreq. +0.05 V vs. normal H electrode and/or pKa3 .ltoreq. 2.0 as necessary requirements for Mn porphyrins to be considered useful SOD mimics.

REFERENCE COUNT: 126 THERE ARE 126 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:311205 CAPLUS

DOCUMENT NUMBER: 130:331880

TITLE: Meso-tetrakis(N-alkylpyridinium)porphyrins and metalloporphyrins as antioxidants

INVENTOR(S): Fridovich, Irwin; Batinic-Haberle, Ines

PATENT ASSIGNEE(S): Duke University, USA

SOURCE: PCT Int. Appl., 81 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9923097	A1	19990514	WO 1998-US23287	19981103
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2309154	AA	19990514	CA 1998-2309154	19981103
AU 9912979	A1	19990524	AU 1999-12979	19981103
AU 737650	B2	20010823		
EP 1045851	A1	20001025	EP 1998-956457	19981103
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001521939	T2	20011113	JP 2000-518967	19981103

Habte

<06/27/2002

US 2002042407 A1 20020411 US 2001-880125 20010614
 PRIORITY APPLN. INFO.: US 1997-64116P P 19971103
 US 1998-184982 B1 19981103
 WO 1998-US23287 W 19981103

OTHER SOURCE(S): MARPAT 130:331880

IT **219818-60-7P**

RL: BAC (Biological activity or effector, except adverse); BSU

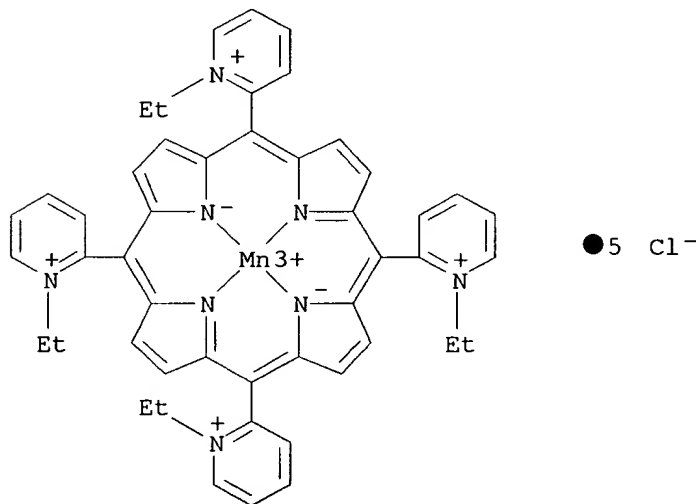
(Biological

study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(atropisomers; prepn., Soret band, redox potential, DNA interaction,
 and superoxide dismutase (SOD) activity as antioxidant)

RN 219818-60-7 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
 .kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
 ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX
 NAME)



IT **223723-81-7 223723-82-8 223723-83-9**

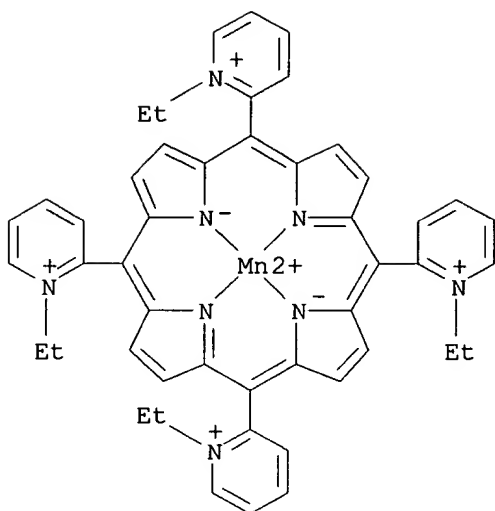
223723-84-0 223723-85-1 223723-86-2

RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation,
 nonpreparative)

(formation in electrochem. redox couple)

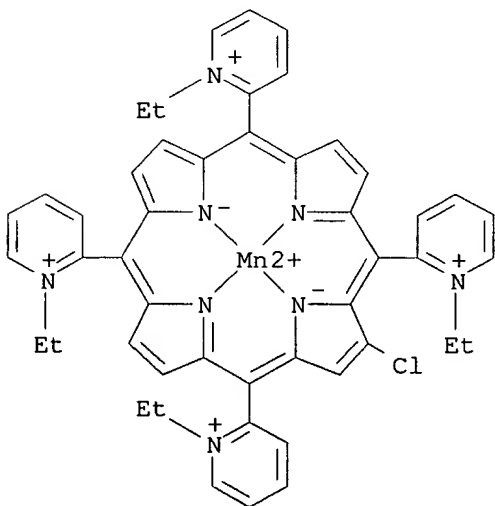
RN 223723-81-7 CAPLUS

CN Manganese(4+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
 .kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
 ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



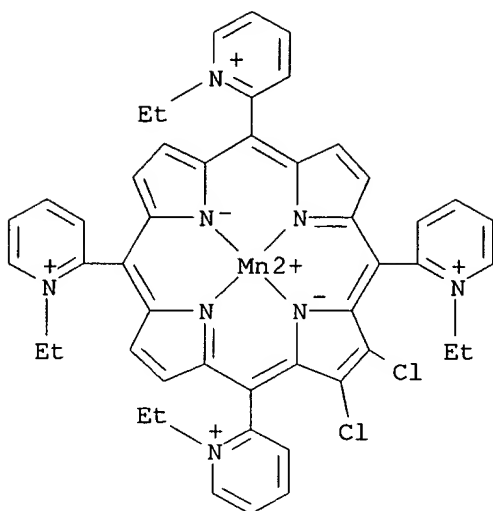
RN 223723-82-8 CAPLUS

CN Manganese(4+), [[2,2',2'',2'''-(2-chloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 223723-83-9 CAPLUS

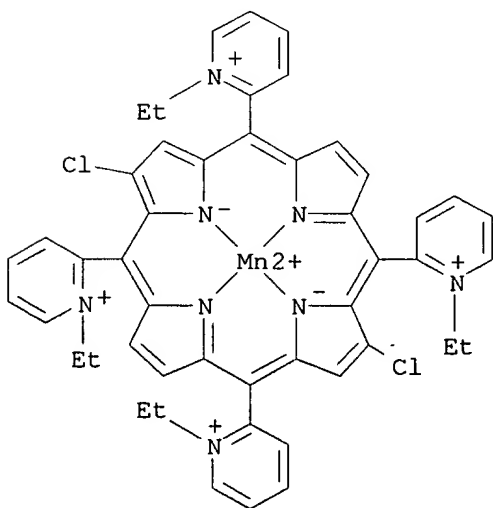
CN Manganese(4+), [[2,2',2'',2'''-(2,3-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 223723-84-0 CAPLUS

CN Manganese(4+),

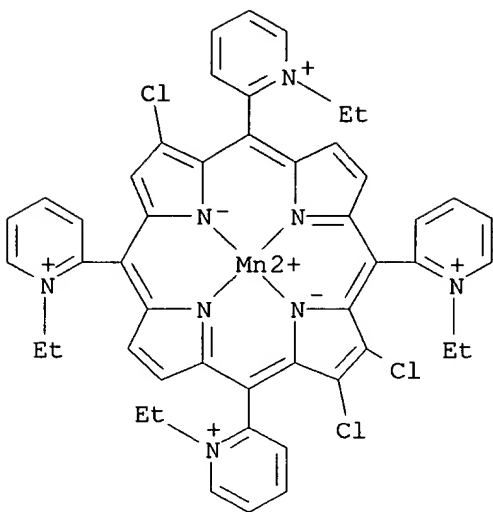
[[2,2',2'',2'''-(2,12-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 223723-85-1 CAPLUS

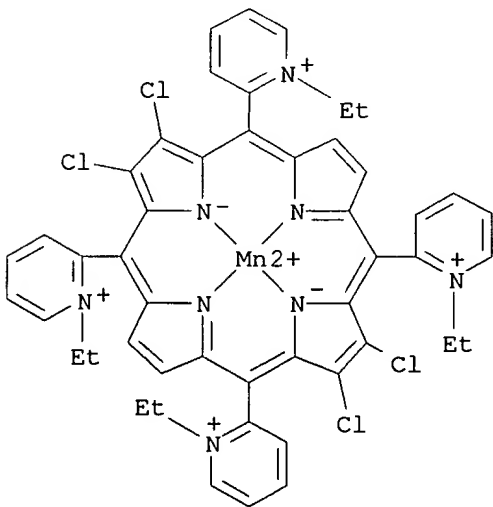
CN Manganese(4+), [[2,2',2'',2'''-(2,3,12-trichloro-21H,23H-porphine-

5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 223723-86-2 CAPLUS

CN Manganese(4+), [[2,2',2'',2'''-(2,3,12,13-tetrachloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)- (9CI) (CA INDEX NAME)



IT 223723-80-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and conversion to chloride salt)

RN 223723-80-6 CAPLUS

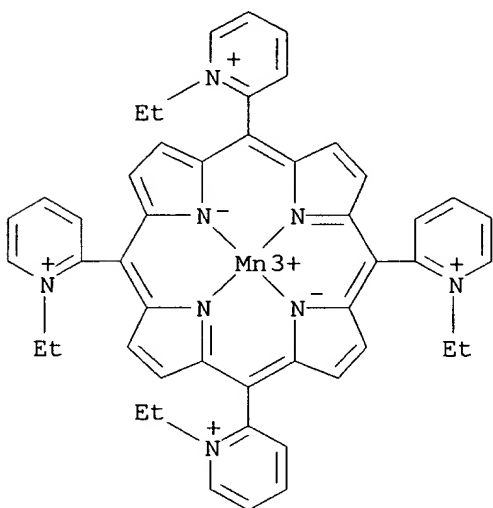
Habte

<06/27/2002

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, (SP-4-1)-, pentakis[hexafluorophosphate(1-)] (9CI) (CA INDEX NAME)

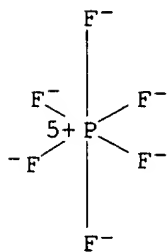
CM 1

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CM 2

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IT 223723-78-2P

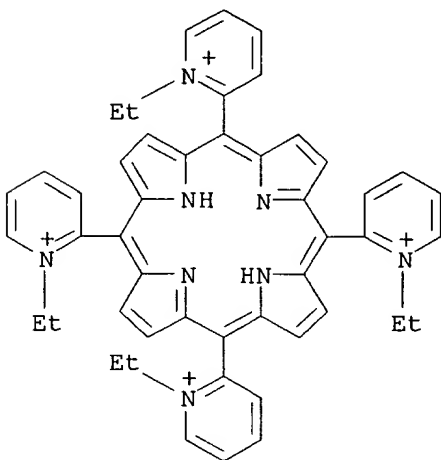
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and metalation with manganese chloride)

RN 223723-78-2 CAPLUS

CN Pyridinium,

2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl)tetrakis[1-ethyl-, tetrachloride (9CI) (CA INDEX NAME)



●4 Cl⁻

IT 219818-71-0P 219818-72-1P

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

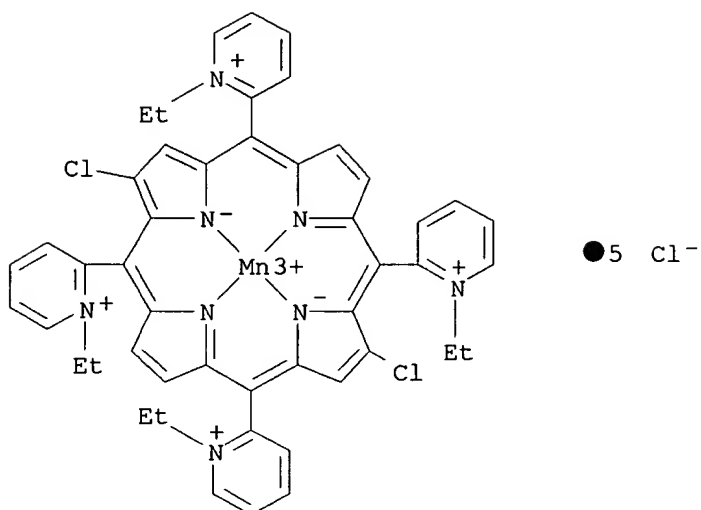
study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. in mixt. with regioisomer, Soret band, redox potential, and superoxide dismutase (SOD) activity as antioxidant)

RN 219818-71-0 CAPLUS

CN Manganese(5+),

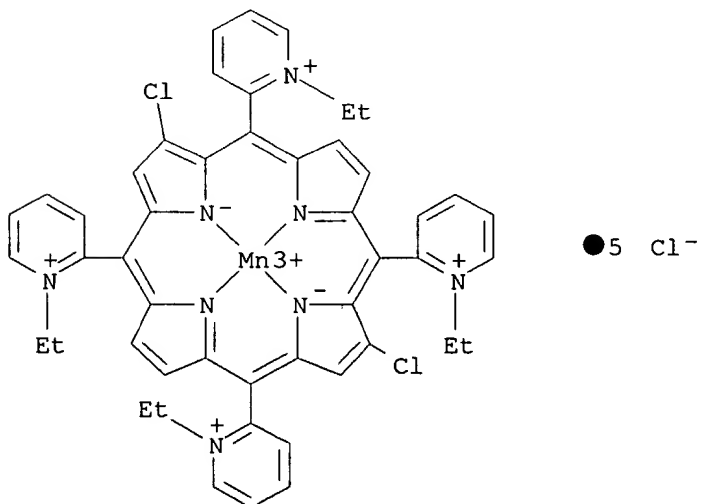
[[2,2',2'',2'''-(2,12-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 219818-72-1 CAPLUS

CN Manganese(5+),

[[2,2',2'',2'''-(2,13-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)



IT 219818-61-8P 219818-62-9P 219818-63-0P

219818-64-1P

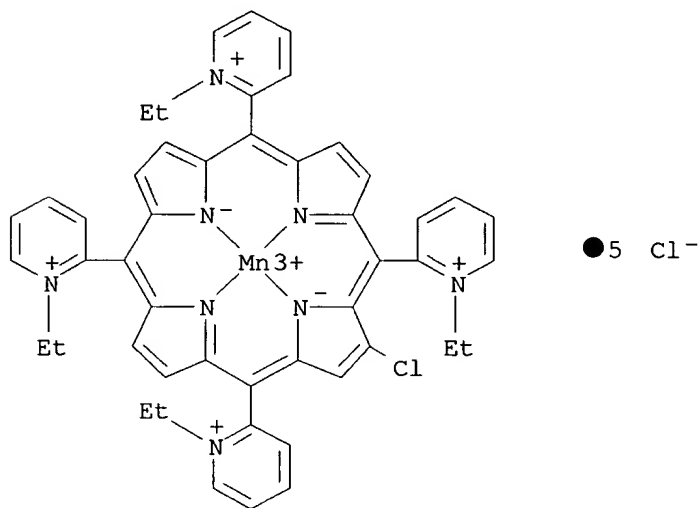
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn., Soret band, redox potential, and superoxide dismutase (SOD) activity as antioxidant)

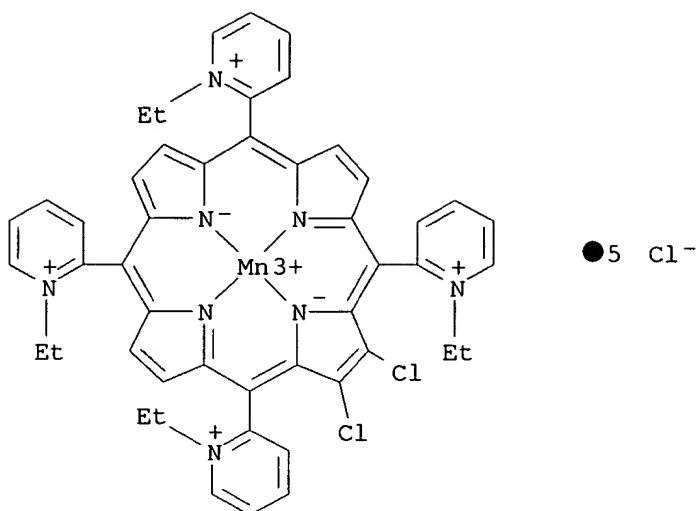
RN 219818-61-8 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2-chloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 219818-62-9 CAPLUS

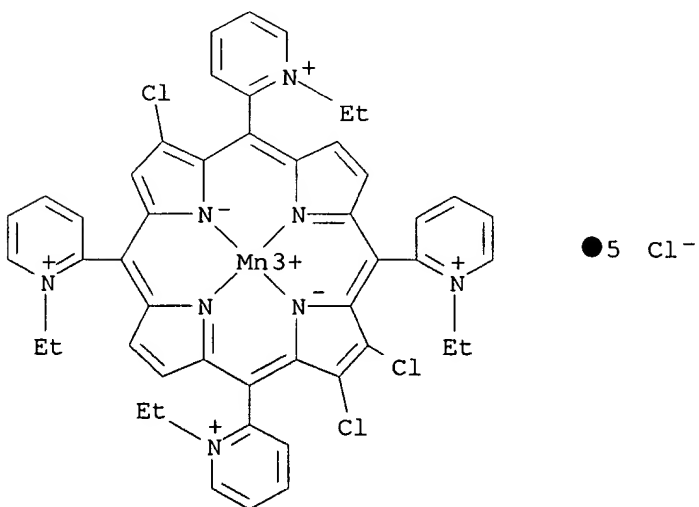
CN Manganese(5+), [[2,2',2'',2'''-(2,3-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 219818-63-0 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2,3,12-trichloro-21H,23H-porphine-

5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)

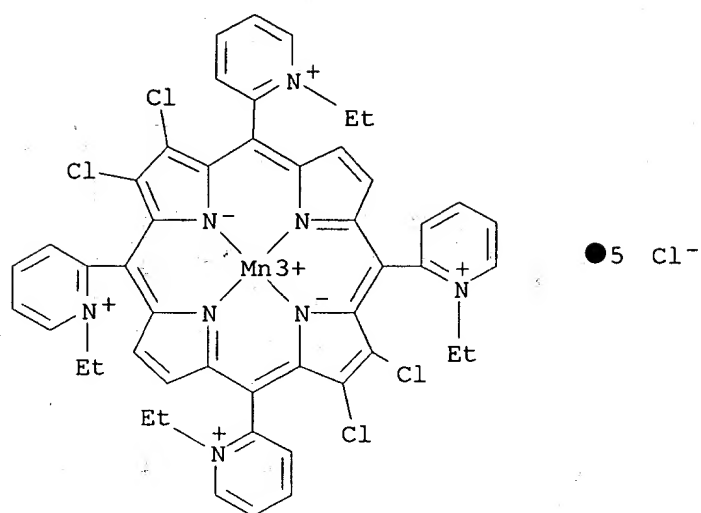


RN 219818-64-1 CAPLUS

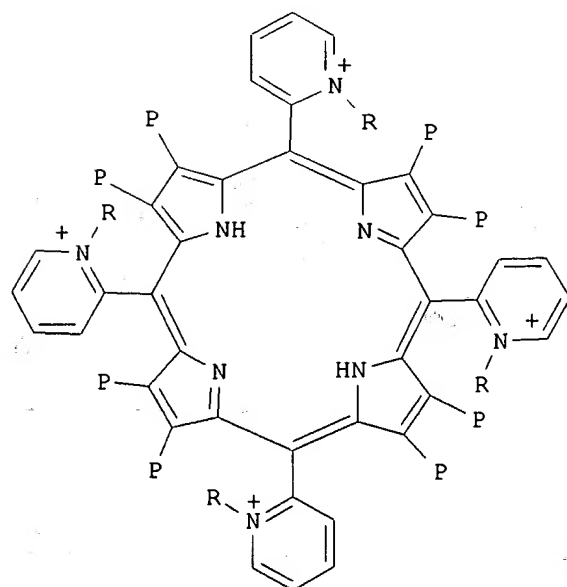
CN Manganese(5+), [[2,2',2'',2'''-(2,3,12,13-tetrachloro-21H,23H-porphine-

5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)

NAME)



GI



I

AB The present invention relates, in general, to a method of modulating

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<06/27/2002

physiol. and pathol. processes and, in particular, to a method of modulating cellular levels of oxidants and thereby processes in which such

oxidants are a participant. The invention also relates to compds. and compns. suitable for use in such methods. Claimed are meso-substituted tetrakis(N-alkylpyridinium-2-yl)porphyrins I (R = C1-8 alkyl, P = electron

withdrawing group or H), their meta-pyridinium analogs, compds. wherein when R = Me and each P = H, the compd. is complexes to Mn, Fe, Cu, Co, Ni,

or Zn, and atropisomer mixts. of the compds. Compds. I, meta-pyridinium analogs, the metal complexes, and pharmaceutically acceptable salts are antioxidants, useful for protecting cells from oxidant-induced toxicity. The same compds. are useful in treating a pathol. condition of a patient resulting from degrdn. of nitrosyl radical or a biol. active form thereof.

Inflammatory lung diseases, including hyper-reactive airway disease and asthma, may also be treated by said compds. Exptl. details for the prepn.

by std. procedures of the substituted porphyrins, chlorinated derivs., and

their metal complexes are given. Reversible metal-centered electrochem. redox behavior was obsd. for all metalloporphyrin products. The metalloporphyrins are potent inhibitors of lipid peroxidn. Superoxide dismutase (SOD) activity studies of the compds. in vitro and in vivo are discussed. A comparison is made of the antioxidant properties of the metalloporphyrins and their redox potentials. The Mn complex of I (R = Et) is demonstrated to be effective in attenuating oxidant stress mediated

by tissue injury and for treatment of bronchopulmonary dysplasia. The effects of the Mn complex of I (R = Me) on vascular tone and in regulation

of airway reactivity are demonstrated.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:807552 CAPLUS

DOCUMENT NUMBER: 130:133157

TITLE: Syntheses and Superoxide Dismuting Activities of Partially (1-4) .beta.-Chlorinated Derivatives of Manganese(III) meso-Tetrakis(N-ethylpyridinium-2-yl)porphyrin

AUTHOR(S): Kachadourian, Remy; Batinic-Haberle, Ines; Fridovich, Irwin

CORPORATE SOURCE: Department of Biochemistry, Duke University Medical Center, Durham, NC, 27710, USA

SOURCE: Inorganic Chemistry (1999), 38(2), 391-396

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

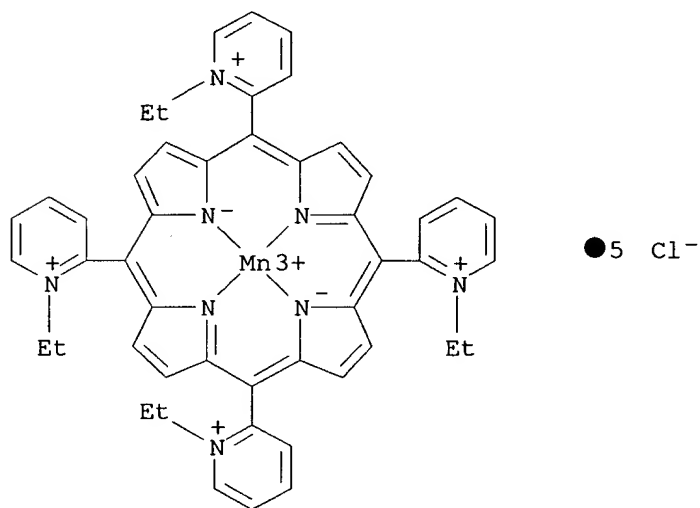
LANGUAGE: English

IT 219818-60-7P 219818-61-8P 219818-62-9P
 219818-63-0P 219818-64-1P 219818-71-0P
 219818-72-1P

RL: CAT (Catalyst use); PRP (Properties); SPN (Synthetic preparation);
 PREP (Preparation); USES (Uses)
 (prepn., redox potentials, and superoxide dismutation catalytic
 kinetics of)

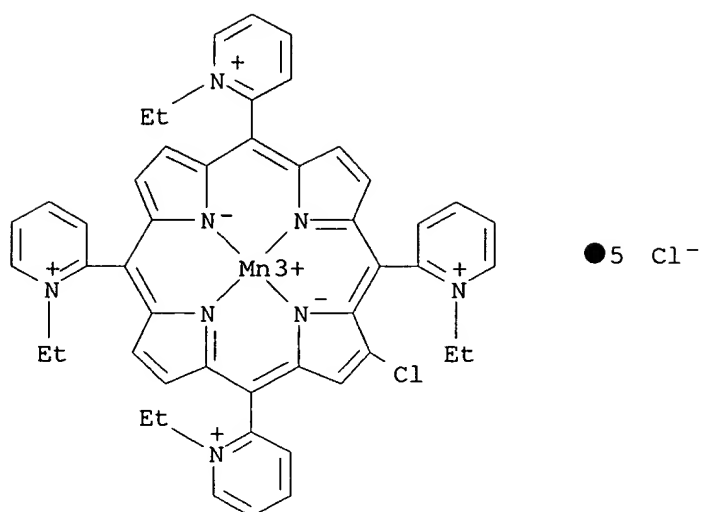
RN 219818-60-7 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(21H,23H-porphine-5,10,15,20-tetrayl-
 .kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-
 ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX
 NAME)



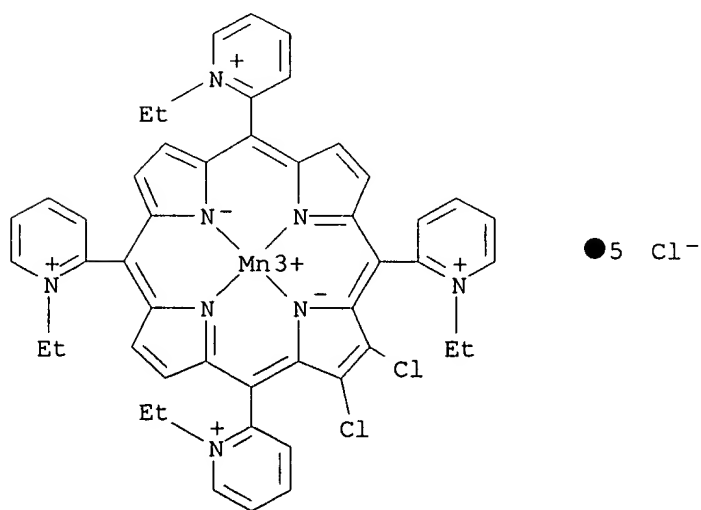
RN 219818-61-8 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2-chloro-21H,23H-porphine-5,10,15,20-
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 ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX
 NAME)



RN 219818-62-9 CAPLUS

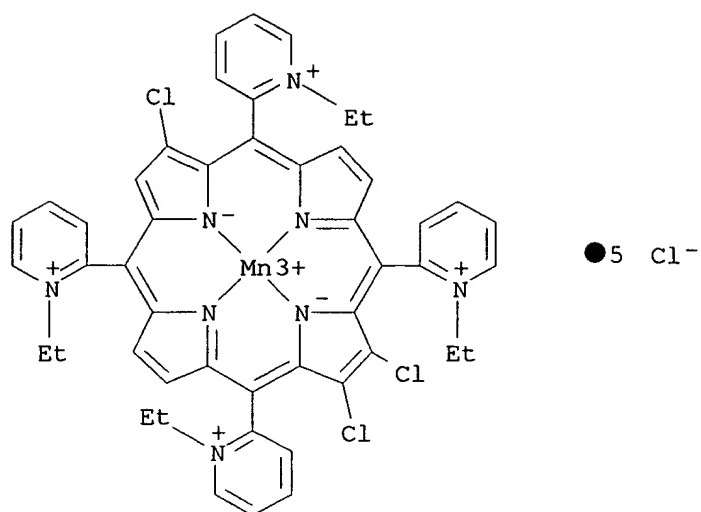
CN Manganese(5+), [[2,2',2'',2'''-(2,3-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 219818-63-0 CAPLUS

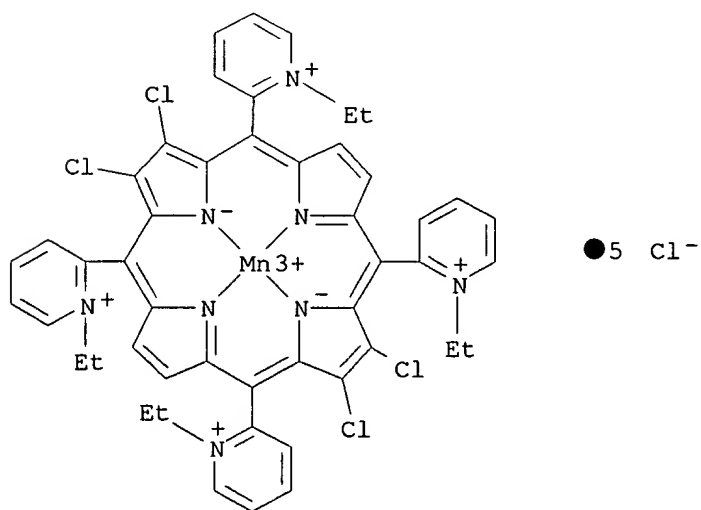
CN Manganese(5+), [[2,2',2'',2'''-(2,3,12-trichloro-21H,23H-porphine-

5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)



RN 219818-64-1 CAPLUS

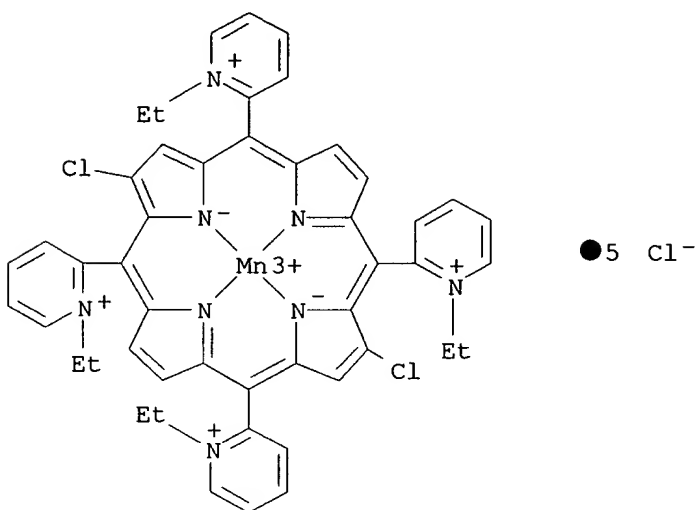
CN Manganese(5+), [[2,2',2'',2'''-(2,3,12,13-tetrachloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-)]-, pentachloride, (SP-4-1)-(9CI) (CA INDEX NAME)



RN 219818-71-0 CAPLUS

CN Manganese(5+), [[2,2',2'',2'''-(2,12-dichloro-21H,23H-porphine-5,10,15,20-

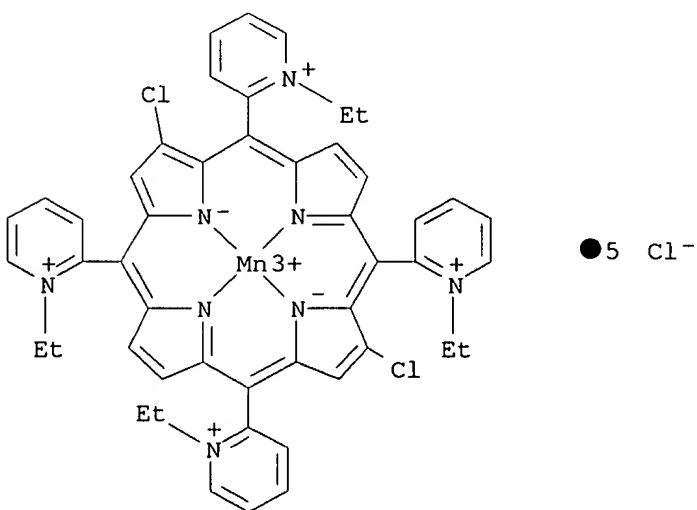
tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-))-, pentachloride, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 219818-72-1 CAPLUS

CN Manganese(5+),

[[2,2',2'',2'''-(2,13-dichloro-21H,23H-porphine-5,10,15,20-tetrayl-.kappa.N21,.kappa.N22,.kappa.N23,.kappa.N24)tetrakis[1-ethylpyridiniumato]](2-))-, pentachloride, (SP-4-2)- (9CI) (CA INDEX NAME)



AB Mn(III) .beta.-mono-, di-, tri-, and tetrachloro-5,10,15,20-tetrakis(N-ethylpyridinium-2-yl)porphyrin (MnCl_xTE-2-PyP5⁺, with x = 1-4) were prepd.

through .beta.-chlorination of 5,10,15,20-tetrakis(2-pyridyl)porphyrin (H₂T-2-PyP) followed by N-ethylation and metalation. Metal-centered redox

potentials and superoxide dismutation activities were measured. Starting from MnTE-2-PyP5⁺, whose redox potential and the related superoxide dismutation activity were E.degree.1/2 = +228 mV vs. normal H electrode and kcat = 5.7 .times. 10⁷ M⁻¹ s⁻¹, resp., the av. increase of 55 mV in the redox potential per added Cl was accompanied by a 65% increase in the rate const. With E.degree.1/2 = +448 mV, the tetrachlorinated deriv. MnCl₄TE-2-PyP5⁺ exhibited the highest superoxide dismuting rate kcat =

4.0

.times. 10⁸ M⁻¹ s⁻¹. The relation between the redox properties (thermodn.

and kinetic factors) and the superoxide dismuting activity of such compds.

is discussed.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:542971 CAPLUS

DOCUMENT NUMBER: 129:170516

TITLE: Porphyrin compounds as telomerase inhibitors

INVENTOR(S): Wheelhouse, Richard T.; Hurley, Laurence H.

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: PCT Int. Appl., 136 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9833503	A1	19980806	WO 1998-US2058	19980204
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9866501	A1	19980825	AU 1998-66501	19980204
EP 988037	A1	20000329	EP 1998-908465	19980204
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
US 6087493	A	20000711	US 1998-18545	19980204

PRIORITY APPLN. INFO.:

US 1997-37295P P 19970205

WO 1998-US2058 W 19980204

OTHER SOURCE(S): MARPAT 129:170516

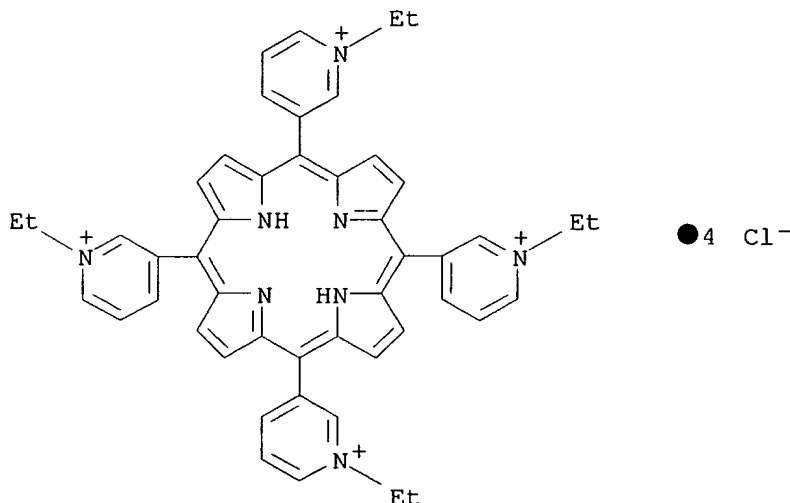
IT 211360-11-1P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (cationic porphyrin compds. as telomerase inhibitors for cancer treatment)

RN 211360-11-1 CAPLUS

CN Pyridinium,

3,3',3'',3'''-(21H,23H-porphine-5,10,15,20-tetrayl)tetrakis[1-ethyl-, tetrachloride (9CI) (CA INDEX NAME)



AB The present invention has identified compds., such as 5,10,15,20-tetra(N-methyl-4-pyridiniumyl)porphine chloride and its metal complexes and related compds., with extended arom. chromophores that bind the G-quadruplex formed by the folding of single-stranded human telomeric DNA.

These compds. are effective telomerase inhibitors and are contemplated to be useful in developing cancer treatments. A model of cationic porphyrin interaction with quadruplex DNA by intercalation was established and in combination with structure activity relations provided novel porphyrin compds. that exhibit discrimination between binding duplex and quadruplex DNA and show improved activity against telomerase. Thus, 5,10,15,20-tetra(N-ethyl-4-pyridiniumyl)porphine chloride (D1) was prepd. in 96% yield by alkylating the pyridinyl analog. D1 shows 55% telomerase inhibition under the conditions described herein.

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

53.06

193.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

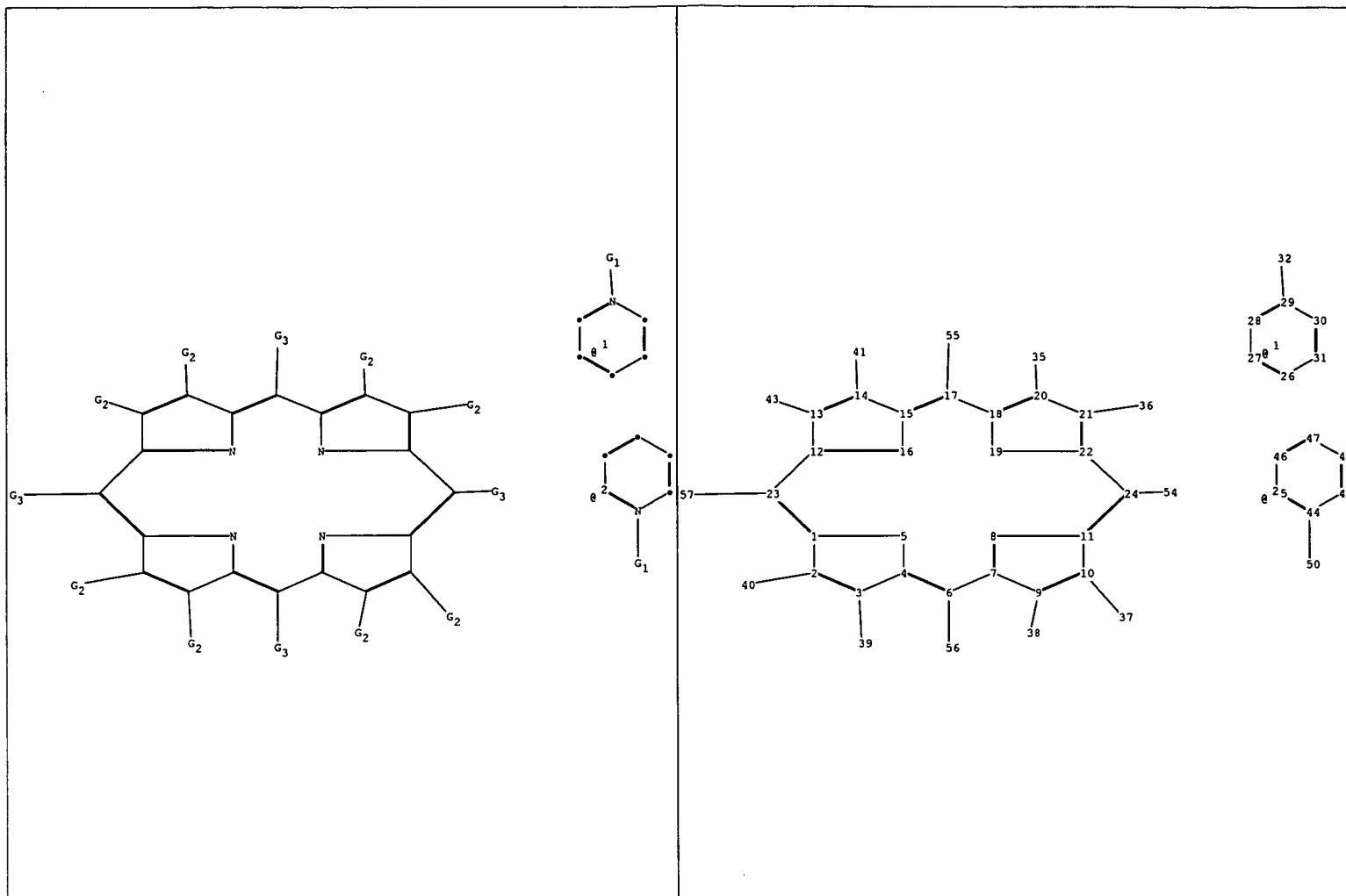
SESSION

CA SUBSCRIBER PRICE

-7.43

-7.43

STN INTERNATIONAL LOGOFF AT 17:00:43 ON 16 JUL 2002



chain nodes :

32 35 36 37 38 39 40 41 43 50 54 55 56 57

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 26
27 28 29 30 31 44 45 46 47 48 49

chain bonds :

2-40 3-39 6-56 9-38 10-37 13-43 14-41 17-55 20-35 21-36 23-57 24-54 29-32
44-50

ring bonds :

1-2 1-5 1-23 2-3 3-4 4-5 4-6 6-7 7-8 7-9 8-11 9-10 10-11 11-24 12-13 12-16
12-23 13-14 14-15 15-16 15-17 17-18 18-19 18-20 19-22 20-21 21-22 22-24 26-27
26-31 27-28 28-29 29-30 30-31 44-45 44-49 45-46 46-47 47-48 48-49

exact/norm bonds :

1-5 2-40 3-39 4-5 6-56 9-38 10-37 13-43 14-41 17-55 18-19 19-22 20-35 21-36
23-57 24-54 29-32 44-50

normalized bonds :

1-2 1-23 2-3 3-4 4-6 6-7 7-8 7-9 8-11 9-10 10-11 11-24 12-13 12-16 12-23
13-14 14-15 15-16 15-17 17-18 18-20 20-21 21-22 22-24 26-27 26-31 27-28 28-29
29-30 30-31 44-45 44-49 45-46 46-47 47-48 48-49

G1:Et,i-Pr

G2:H,X

G3:[*1],[*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS 43:CLASS 44:Atom
45:Atom